

# Sensitivity of 3D gradient recalled echo susceptibility-weighted imaging technique compared to computed tomography angiography for detection of middle cerebral artery thrombus in acute stroke

Amit Agarwal,<sup>1</sup> Kanupriya Vijay,<sup>1</sup>  
Krishnamoorthy Thamburaj,<sup>1</sup>  
Sangam Kanekar,<sup>2</sup> Paul Kalapos<sup>3</sup>

<sup>1</sup>Department of Radiology, <sup>2</sup>Department of Neurology and Radiology,

<sup>3</sup>Department of Neurosurgery and Radiology, Penn State University, Hershey Medical Center, PA, USA

## Abstract

We aimed at comparing the sensitivity of magnetic resonance (MR) susceptibility-weighted imaging (SWI) with computed tomography angiography (CTA) in the detection of middle cerebral artery (MCA) thrombus in acute stroke. Seventy-nine patients with acute MCA stroke was selected using our search engine software; only the ones showing restricted diffusion in the MCA territory on diffusion-weighted images were included. We finally selected 35 patients who had done both MRI (including SWI) and CTA. Twenty random subjects with completely normal MRI (including SWI) exam were selected as control. Two neuroradiologists (blinded to the presence or absence of stroke) reviewed the SW images and then compared the findings with CT angiogram (in patients with stroke). The number of MCA segments showing thrombus in each patient was tabulated to estimate the thrombus burden. Thrombus was detected on SWI in one or more MCA segments in 30 out of 35 patients, on the first review. Of the 30, SWI showed thrombus in more than one MCA segments in 7 patients. CTA depicted branch occlusion in 31 cases. Thrombus was seen on both SWI and CTA in 28 patients. Thrombus was noted in two patients on SWI only, with no corresponding abnormality seen on CTA. Two patients with acute MCA showed no vascular occlusion or thrombus on either CTA or SWI. Only two case of false-positive thrombus was reported in normal control subjects. Susceptibility-weighted images had sensitivity and specificity of 86% and 90% respectively, with positive predictive value 94%. Sensitivity was 86% for SWI, compared with 89% for CTA, and this difference was statistically insignificant ( $P>0.05$ ). Of all the positive cases on CTA (31) corresponding thrombus was seen on SWI

in 90% of subjects (28 of 31). Susceptibility-weighted imaging has high sensitivity for detection of thrombus in acute MCA stroke. Moreover, SWI is a powerful technique for estimation of thrombus burden, which can be challenging on CTA.

## Introduction

The demonstration and location of arterial occlusion may have prognostic and therapeutic implications in acute stroke patients. The diagnosis of arterial occlusion is usually made on computed tomography (CT) or magnetic resonance (MR) angiography. MRI is increasingly being used as the sole modality for the emergency imaging of patients with suspected acute stroke, whether ischemic or hemorrhagic, and might increase the cost-effectiveness of stroke care. Three-dimensional gradient recalled echo (3D-GRE) susceptibility-weighted imaging (SWI) is a new high-resolution imaging MR technique that amplifies phase to enhance the magnitude contrast and susceptibility differences between tissues. This is exquisitely sensitive to venous blood, hemorrhages and iron storage and is commonly used in traumatic brain injuries and for high resolution brain venographies. SWI has also developed into a powerful clinical tool for MR imaging of acute stroke, with many added advantages over T2\*-GRE imaging. One of the useful clinical applications of SWI is detection intravascular clot at the acute stage, especially distally located clots, which may be missed by angiography. We have been using this new sequence in our hospital to evaluate patients with acute stroke, with high sensitivity for detection of the intra-arterial thrombus. In this paper, we retrospectively review 35 cases that underwent CT and MRI (including SWI) for their initial evaluation of stroke and compare the sensitivity of CTA and SWI in detection of thrombus. In addition, we evaluated the usefulness of SWI to assess the thrombus burden.

## Materials and Methods

The University Institutional Review Board approved the study. A series of 79 patients with acute middle cerebral artery (MCA) stroke was selected using *MCA infarct* in our search engine software (Primordial Design, Inc. San Mateo CA, USA); under the time frame of January 2009 to May 2012. Inclusion criteria were: i) diffusion positive cases of acute onset MCA infarct, ii) CT angiogram of the brain and MRI performed within 48 hours of clinical onset, iii) SWI included in the MRI protocol. All patients with SWI, included in our study, had

Correspondence: Amit Agarwal, Department of Radiology, Penn State University, Hershey Medical Center, 500 University Drive, Hershey, PA 17036, USA.  
Tel.: +1.717.531.6737 - Fax: +1.717.531.0006.  
E-mail: aagarwall@hmc.psu.edu

Key words: stroke, susceptibility-weighted imaging, thrombus, computed tomography.

Contributions: the authors contributed equally.

Conflict of interests: the authors declare no potential conflict of interests.

Received for publication: 16 June 20014.  
Accepted for publication: 11 August 2014.

This work is licensed under a Creative Commons Attribution NonCommercial 3.0 License (CC BY-NC 3.0).

©Copyright A. Agarwal et al., 2014  
Licensee PAGEPress, Italy  
Neurology International 2014; 6:5521  
doi:10.4081/ni.2014.5521

Minimum Intensity Projection (mIP) images which was used for detection of thrombus. Exclusion criteria were: i) multi-territorial infarcts, including embolic infarcts and vasculitic infarcts, ii) poor quality SWI due to motion artifacts, iii) watershed infarcts, iv) acute lacunar infarcts and other small infarcts which could not be definitely classified as MCA territorial infarcts and, v) hemorrhagic infarcts. CT angiogram was performed on a Siemens Definition 64 slice dual tube CT scanner. MRI was done on either 1.5 or 3-Tesla Siemens Magnetom Vision (Siemens, Munich, Germany). The interval between CT and MR imaging ranged from 4 hours to 41 hours (mean, 29 hours 36 minutes). We finally had 35 patients who satisfied all the criteria. All of these patients were evaluated with the new 3D-GRE SWI MR technique in addition to other conventional MRI techniques, including DWI with apparent diffusion coefficient (ADC) maps. The SWI acquisition time was 4 minutes 47 seconds. SW images were created using the magnitude and phase raw data sets. A phase mask was created by setting all positive phase values (between 1 and 180°) to unity and by normalizing the negative phase values ranging from 0 to -180° to a gray scale of values ranging linearly from unity to zero, respectively. This normalized phase mask was multiplied four times against the original magnitude image and yielded images that enhanced the hypointensities of the region containing susceptibility properties (deoxygenated venous blood, clot, and hemosiderin). Finally, a minimum intensity projection (mIP) over two slices was performed to display the processed data

using contiguous sections of 4-mm thickness in the axial plane. The processing was done automatically within the Siemens Vision software. All the cases, which were finally included in our study, were reviewed by two fellowship trained Neuroradiologists (A.K.A and S.G.K).

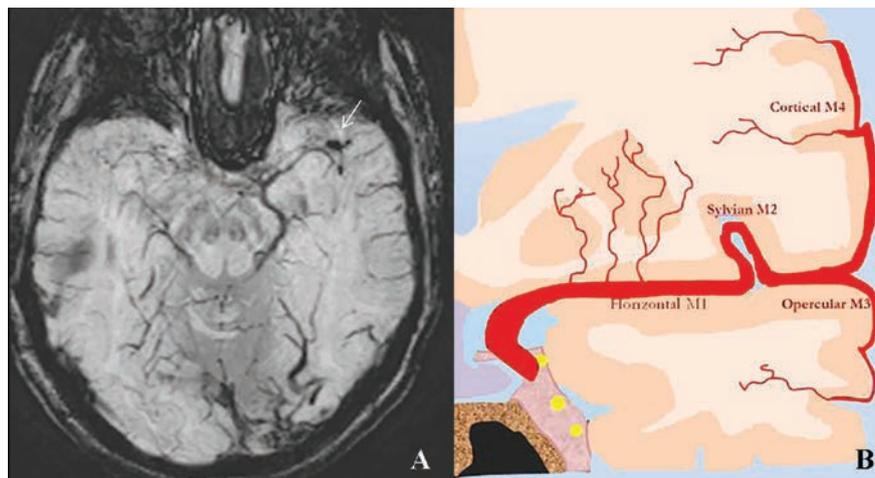
We first reviewed the SWI-mIP images only, being completely blinded to the clinical history and other imaging sequences. The reviewers however knew that all the cases being reviewed had either Diffusion positive acute MCA infarct or were unremarkable. The presence of clot was seen as hypointensity within MCA, in which the diameter of the hypointense signal within the vessel exceeded the contralateral vessel diameter (Figure 1A). Observations were made for the presence of MCA thrombus, extent of thrombus, and segments of MCA involved. The four MCA segments included M1: from the origin to bifurcation/trifurcation, M2: from bi (tri) furcation to origin of cortical branches, M3: opercular branches (those within the sylvian fissure) and M4: branches emerging from the sylvian fissure onto the surface of the hemisphere (Figure 1B). Following these observations, other MR sequences including DWI and the CT angiogram of the brain were reviewed. Again, mutual consensus was obtained between the reviewers, regarding the presence and location of branch occlusion. At this time, however, the reviewers knew the side and exact location of the infarct. A second review of the SWI was made after evaluation of CTA. However, this data was not used for statistical evaluation of the sensitivity and specificity of SWI.

## Results

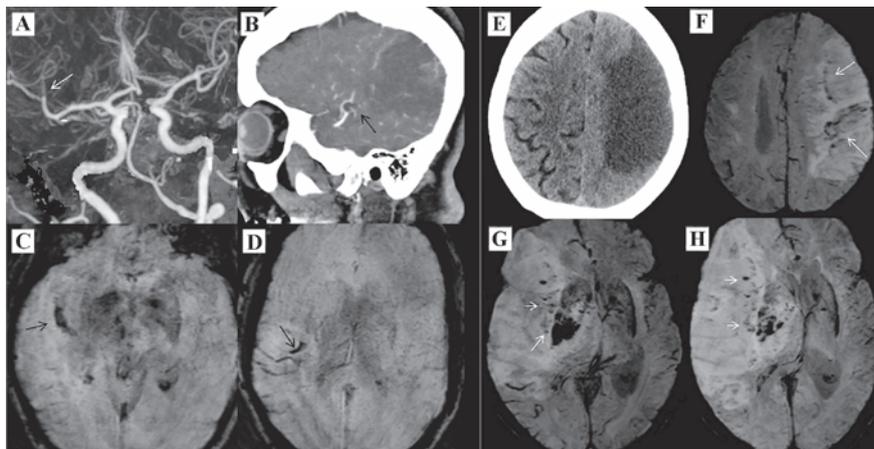
The clinical and imaging standard for our study was the presence of DWI positive MCA infarct. Intra-arterial MCA thrombus was seen on SWI in thirty cases (86%) of the 35 reviewed (Table 1). Of the 30, SWI showed thrombus in more than one MCA segments in 7 patients (Figure 2A-D). M1 segment was most commonly involved, with thrombus seen in this segment in 19 of 30 cases. Thrombus was seen in the M2 segment in 12 cases. One patient had involvement of the opercular M3 MCA segment. Six-patients had involvement of the cortical M4 branch of MCA. We excluded any case with frank hemorrhagic transformation from our study; however, few scattered foci of petechial hemorrhages (Figure 2E-H) were seen in 13 cases (37%). More than 50% of cases positive for branch occlusion on CTA had poor distal reconstitution (Figure 3A-C). Estimation of thrombus burden or the number of MCA segments involved was therefore difficult for most cases on CTA. Thrombus was noted in two patients on SWI only, with no cor-

responding abnormality seen on CTA. Both these patients had branch occlusion of distal M4 segment of MCA. Two patients with acute MCA infarct showed no vascular occlusion or thrombus on either CTA or SWI. Only two case

of false-positive thrombus was reported in normal control subjects (n=20). False-positive thrombus was seen in the M1 segments in both these patients. The sensitivity of SWI versus CT angiogram for thrombus detection was



**Figure 1.** A) Thrombotic occlusion of the M2 division of the left MCA in a 52 year-old female presented with right-sided numbness, slurred speech. The presence of clot (arrow) is seen as hypointensity within MCA, with the diameter of the hypointense signal being larger than the diameter of adjacent and contralateral vessels. B) The four MCA segments include M1: from the origin to bifurcation, M2: from bi (tri) furcation to origin of cortical branches, M3: opercular branches (those within the sylvian fissure) and M4: branches emerging from the sylvian fissure onto the surface of the hemisphere.



**Figure 2.** A-D) A 63-year-old female presenting with acute left-sided weakness. A) CT angiogram (MIP image) shows abrupt complete occlusion (white arrow) of posterior M2 branch of the right MCA, with poor visualization of distal branches. B) Sagittal CTA images, shows the location of vascular occlusion (black arrow), however presence of any distal clot/branch occlusion cannot be ascertained. C) SW-mIP axial images show the main intra-arterial clot in the posterior M2 branch of MCA (black arrow), corresponding to the CTA findings. D) A second distal clot is noted in the M4 cortical branch on the same side (black arrow). This was not seen on CTA even after retrospective evaluation. E-H) Cases with frank hemorrhagic transformation were excluded from our study; however, few scattered foci of petechial hemorrhages were seen in 13 cases (37%). E) Unenhanced head CT in a 82 year old shows acute infarct in left MCA territory with no hemorrhagic transformation. F) SW images from subsequent MRI performed after 5 hours shows multiple cortical petechial hemorrhages (arrows). G,H) Frank hemorrhagic transformation in 63 year old with right MCA infarct. Even in patients with frank hemorrhagic transformation, the extent of hemorrhage and present of other microbleeds (arrows) was better assessed on SWI (compared to CT).

calculated at 86% and 89% respectively, with positive predictive value 94% (Table 2). Using CT as the clinical standard for detection of thrombus in acute stroke, SWI demonstrated 90% relative sensitivity (28 of 31 cases positive on CTA was also positive on SWI). Eleven patients underwent catheter guided intra-arterial thrombolysis. All these patients who had therapeutic intervention had either stem MCA occlusion or occlusion of both M1 and M2 segments.

## Discussion

Despite an ongoing controversy over the utility of MRI, the advent of new MRI techniques, such as perfusion-imaging (PI) and DWI has had a significant impact on diagnostic imaging in acute ischemic stroke.<sup>1</sup> In one of the largest pooled multicenter analysis of 1210 thrombolysed patients, Schellinger *et al.*<sup>2</sup> concluded that MRI-based thrombolysis is safer and more effective than standard CT-based thrombolytic therapy for acute ischemic stroke. It does not cause a significant time loss, and the type of patients selected by this algorithm seems to be fairly homogeneous among different centers. The positive impact of MRI-based patient selection is accentuated beyond the 3-hour time window. Since MRI using DWI is more sensitive than CT for the detection of acute infarct, it would be advantageous to use MRI to also exclude the presence of acute hemorrhage within an acute infarct. In addition, chronic small brain hemorrhages are not well detected by CT, but are detected on MRI, particularly T2\*-GRE sequences. This provides an additional theoretical benefit of MRI over CT for scanning candidates for thrombolytic therapy.<sup>3</sup> Although DWI and PI are powerful methods for detecting acute cerebral ischemia, new techniques such as SWI may be used as an adjunct to characterize the affected vascular territory further. Susceptibility-weighted imaging (SWI) consists of using both magnitude and phase images from a high-resolution, three-dimensional, fully velocity compensated gradient-echo sequence. SWI is currently being tested in a number of centers worldwide as an emerging technique to improve the diagnosis of neurological trauma, brain neoplasms, and neurovascular diseases because of its ability to reveal vascular abnormalities and microbleeds.<sup>4</sup> There are 3 components to interpret in the SWI data to make a clinical diagnosis (Figure 3D-F). The first component is the magnitude image, which has poor blooming effect because of high resolution.<sup>5</sup> The second component to interpret in SWI data is the phase image. For a right-handed system, veins will look dark on the phase image (because the

**Table 1. Segments of middle cerebral artery thrombus on susceptibility-weighted images (30 patients).**

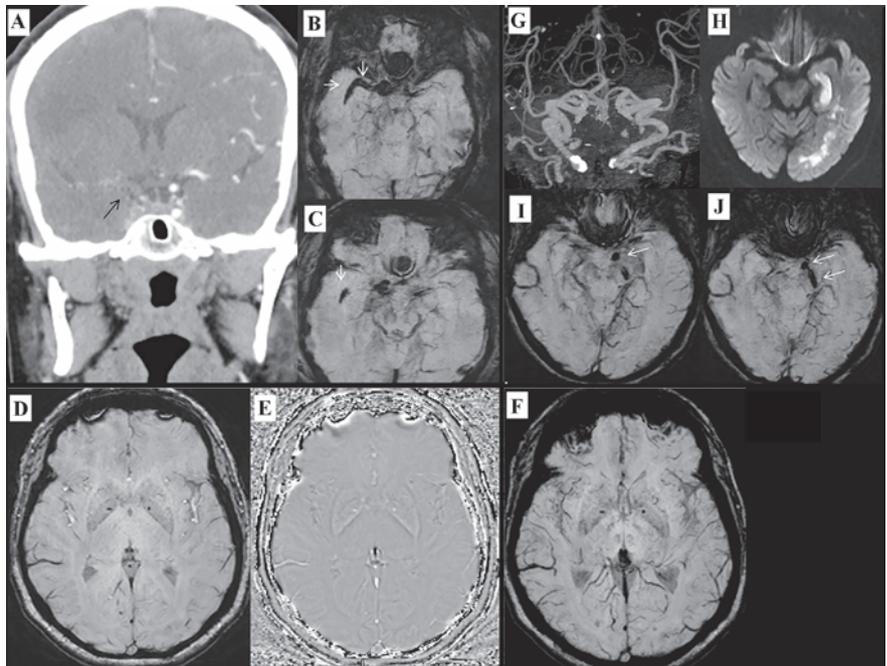
Segments	N.	%
Isolated M1 segment (including stem occlusion)	19	63
Isolated M2 segment	12	40
Isolated M3 segment	1	3
Isolated M4 segment	6	20
Two MCA segments *	6	20
Three MCA segments**	1	3

MCA, middle cerebral artery. \*Three had involvement of M1 and M2 segments, two had involvement of M2 and M4 segments and one had involvement of M1 and M4 segments. \*\*Thrombus was seen in M1, M2 and M4 segment

**Table 2. Sensitivity and specificity of susceptibility-weighted images for intra-arterial clot.**

	Diffusion positive MCA infarct (n=35)	Control (n=20)
SWI positive	30 (true positive)	2 (false positive)
SWI negative	5 (false negative)	18 (true negative)

SWI, susceptibility-weighted images; MCA, middle cerebral artery. Sensitivity: 86%, Specificity: 90%, PPV: 94%.



**Figure 3.** A-C) A 52-year-old female presenting with acute left-sided weakness. A) CT angiogram (MIP image) shows non-visualization of the right ICA and the MCA (arrow) with no reconstitution of the distal branches. The presence and extent of thrombus into the MCA cannot be delineated on CTA. B, C) Two contiguous SW-mIP axial images show the *blooming* effect from the intra-arterial PCA clot. The entire extent of the thrombus can be accurately delineated. The thrombus is seen extending along the entire M1 segment and a good part of the posterior M2 segment (arrows). D-F) There are 3 components to interpret in the SWI data to make a clinical diagnosis. The first component is the magnitude image (D), which has poor blooming effect because of high resolution. The second component to interpret in SWI data is the phase image (E). The veins will look dark on the phase image because the deoxygenated blood is paramagnetic relative to its surrounding tissue (right-handed system). The third component used in interpreting SWI is the final processed SWI, using mIP technique (F). Given the high blooming effect, we used mIP images for thrombus detection in our study. G-J) A 68-year-old female presenting with acute facial droop and visual changes. G) CT angiogram (MIP image) shows abrupt complete occlusion (arrow) of left posterior cerebral artery (PCA) with no reconstitution of the distal branches. H) DW images shows restricted diffusion in the left PCA territory. I, J) Two contiguous SW-mIP axial images show the *blooming* effect from the intra-arterial PCA clot (arrows). As with MCA thrombus, the estimation of thrombus extent is limited on CT angiogram (secondary to poor reconstitution of distal branch) however is clearly delineated on the SW images.

deoxygenated blood is paramagnetic relative to its surrounding tissue) and calcium will look bright (because calcium is diamagnetic relative to the brain tissue).<sup>6</sup> The third component used in interpreting SWI is the final processed SWI, using mIP technique. These data have taken full advantage of T2\* signal-intensity losses in the magnitude image and iron increases in the phase images to highlight both types of contrast in a single image.<sup>7</sup> Given the high blooming effect, we used mIP images for thrombus detection in our study.

In 2000, Flacke *et al.*<sup>8</sup> compared the sensitivities of susceptibility-based perfusion MR imaging and hyperdense MCA sign at CT, for detection of acute thrombus in MCA stroke. The location and approximate size of thrombus was readily depicted in 9 of 11 patients, with a sensitivity of 82 %. They concluded that detection of the thrombus was an additional benefit from perfusion MR imaging without prolonging the total examination time. Our study included a larger subject size and used dedicated 3D-GRE susceptibility-weighted images with magnitude and phase images along with processed mIP images. In our study the sensitivity of SWI images approached 86%, which was higher than susceptibility-based perfusion MR imaging. Our method does prolong the examination time, however with many other added benefits of SWI, this new technique is replacing T2\*-GRE images at many centers, included our center, even for MR stroke protocols. The current scan time using SWI is somewhat long, 5-8 minutes for thirty-two 2-mm slices. Further improvements in speed by a factor of 2-4 with segmented echo-planar imaging or a factor of 2-3 with parallel imaging are possible. Once these methods are available, either faster imaging times or greater volume coverage will be possible.<sup>2</sup> The *susceptibility sign* on MR images is defined as presence of hypointensity within the Internal carotid artery (ICA) or MCA, in which the diameter of the hypointense signal within the vessel exceeded the contralateral vessel diameter.<sup>9</sup> Fresh clots contain a high concentration of deoxyhemoglobin and appear hypointense on SWI.<sup>10</sup> In 2006, Kim *et al.*<sup>11</sup> studied the sensitivity of middle cerebral artery susceptibility sign on T2\*-weighted images and its effect on recanalization and clinical outcome after thrombolysis. In this study, positive MCA susceptibility sign on the initial T2\*-weighted imaging was detected in 16 (48%) of the 33 patient. This is significantly lower than the sensitivity of MCA *susceptibility sign* in our study, using 3D SW images as compared to T2\*-GRE (used in the study by Kim *et al.*). Many other benefits of SWI have been extensively studied and include: i) detecting a hemorrhagic component within the region of infarction, further helping to distinguish ischemic and hemorrhagic stroke; ii) demon-

strating areas of hypoperfusion and directing the necessity of perfusion imaging; and iii) predicting the probability of potential hemorrhagic transformation before thrombolytic treatment by counting the number of microbleeds and early detection of hemorrhagic complication after intra-arterial thrombolysis.<sup>5</sup> Another significant observation in our study was the estimation of thrombus extent/burden using segmental analysis of thrombotic MCA occlusion. Several studies and clinical trials have established the importance of clot burden in the prediction of stroke outcome.<sup>12</sup> In 2008, Puetz *et al.*<sup>13</sup> showed in their research study (on 263 patients) how quantification of intracranial thrombus extent with the clot burden score can predict functional outcome, final infarct size and parenchymal hematoma risk. The effects of clot burden have been indirectly examined via the hyperattenuated arterial sign on non-contrast CT and directly via conventional and CT angiographic studies with variable results.<sup>14</sup> In our study, there was involvement of more than one MCA segments in 20% patients. SW images show higher sensitivity for estimation of clot extent, especially in distal branches, which can be challenging on CT angiogram. Although, we did not perform quantitative estimation of clot burden by definitive measurement of clot size, the number of segments involve does provide a rough assessment. Larger studies are needed to address the accuracy of SWI for quantitative estimation of clot burden.

A potential benefit of SWI may be the detection of distally located clots, which may be missed by CTA.<sup>15</sup> Two patients in our study showed thrombus in the distal M4 segment on SWI only, with no corresponding abnormality seen on CTA. Given the high sensitivity of SWI for intra-arterial clot, this could be potentially be used for other territorial infarcts, especially posterior circulation infarct (Figure 3G-J). Although we excluded patient with frank hemorrhagic transformation from our study, 33% of patients with acute infarct in our study has petechial foci of hemorrhage on SWI. This is similar to the findings by Wycliffe *et al.*,<sup>2</sup> who observed a sensitivity of 42% for SWI detection of parenchymal hemorrhage in acute MCA stroke, which was significantly higher than conventional MRI or CT. Even though some of the patients will probably not develop prominent hemorrhage in spite of small amounts of detectable hemorrhage in the initial SWI, CT scan is grossly inadequate in detection of true significant incidence of hemorrhage in acute stroke on the initial evaluation. There are several potential sources of bias in this study. First, this was not a prospective or randomized study. Sensitivity of SWI was calculated on the assumption that all patients with Diffusion positive MCA infarct have arterial thrombus. Both 1.5 and 3T magnets were used for MR

acquisition which could result in difference in sensitivities of SWI. We used the number of MCA segments involved to estimate the thrombus burden, which may not be as accurate as quantitative measurement of thrombus size. In a number of cases, demarcation of intra-arterial clot from cortical and subarachnoid hemorrhages may be difficult, especially in distally located clots. Finally, the sensitivity for thrombus detection may be different in patients with Transient ischemic attacks (TIAs), as all the patients in our study had already infarcted. Further prospective studies are warranted in a larger patient population.

## Conclusions

In summary, these data demonstrate that SWI is a very sensitive tool for detection of intra-arterial thrombus in acute MCA stroke, compared with other techniques including CT Angiography. Moreover, SWI can provide an accurate estimation of thrombus burden. Further investigation is needed with well-designed prospective studies to confirm these findings. Addition of SWI sequence in evaluation of acute stroke may make MRI adequate for evaluation regarding thrombolytic therapy and may eliminate the need for CT to detect hemorrhage in acute stroke.

## References

- Schellinger PD, Fiebich JB, Marler OJ. Stroke magnetic resonance imaging within 6 hours after onset of hyperacute cerebral ischemia. *Ann Neurol* 2001;49:460-9.
- Schellinger PD, Thomalla G, Fiehler J, et al. MRI-based and CT-based thrombolytic therapy in acute stroke within and beyond established time windows: an analysis of 1210 patients. *Stroke* 2007;38:2640-5.
- Wycliffe ND, Choe J, Holshouser B, et al. Reliability in detection of hemorrhage in acute stroke by a new three-dimensional gradient recalled echo susceptibility-weighted imaging technique compared to computed tomography: a retrospective study. *J Magn Reson Imaging* 2004;20:372-7.
- Sehgal V, Delproposito Z, Haacke M, et al. Clinical applications of neuroimaging with susceptibility-weighted imaging. *J Magn Reson Imaging* 2005;22:439-50.
- Mittal S, Wue DZ, Neelavallib J, et al. Susceptibility-weighted imaging: technical aspects and clinical applications. Part 2. *Am J Neuroradiol* 2009;30:232-52.
- Haacke EM, Mittal S, Wu Z, et al. Susceptibility-weighted imaging: techni-

- cal aspects and clinical applications. Part 1. *Am J Neuroradiol* 2009;30:19-30.
7. Du YP, Jin Z. Simultaneous acquisition of MR angiography and venography (MRAV). *Magn Reson Med* 2008;59:954-8.
  8. Flacke S, Urbach H, Keller E, et al. Middle cerebral artery (MCA) susceptibility sign at susceptibility-based perfusion MR imaging: clinical importance and comparison with hyperdense MCA sign at CT. *Radiology* 2000;215:476-82.
  9. Rovira A, Orellana P, Alvarez-Sabin J, et al. Hyperacute ischemic stroke: middle cerebral artery susceptibility sign at echo-planar gradient-echo MR imaging. *Radiology* 2004;232:466-73.
  10. Chalela JA, Haymore JB, Ezzeddine MA, et al. The hypointense MCA sign. *Neurology* 2002;58:1470.
  11. Kim HS, Lee DH, Choi CG, et al. Progression of middle cerebral artery susceptibility sign on T2\*-weighted images: its effect on recanalization and clinical outcome after thrombolysis. *Am J Roentgenol* 2006;187:650-7.
  12. Sillanpaa N, Saarinen JT, Rusanen H, et al. The clot burden score, the Boston Acute Stroke Imaging Scale, the cerebral blood volume ASPECTS, and two novel imaging parameters in the prediction of clinical outcome of ischemic stroke patients receiving intravenous thrombolytic therapy. *Neuroradiology* 2012;54:663-72.
  13. Puetz V, Dzialowski I, Hill MD, et al. Intracranial thrombus extent predicts clinical outcome, final infarct size and hemorrhagic transformation in ischemic stroke: the clot burden score. *Int J Stroke* 2008;3:230-6.
  14. Riedel CH, Jensen U, Rohr A, et al. Assessment of thrombus in acute middle cerebral artery occlusion using thin-slice non-enhanced computed tomography reconstructions. *Stroke* 2010;41:1659-64.
  15. Hermier M, Nighoghossian N. Contribution of susceptibility-weighted imaging to acute stroke assessment. *Stroke* 2004;35:1989-94.